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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/484,048	01/18/2000	Stig Steen	33314WC548931	9191

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EXAMINER

AFREMOVA, VERA

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 11/03/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/484,048

Applicant(s)

STEEN, STIG

Examiner

Vera Afremova

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 July 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1,4-7 and 24-35 is/are pending in the application.
- 4a) Of the above claim(s) 4 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1,5-7 and 24-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 09/093,614.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/14/2003 has been entered.

Status of claims

Claims 1, 5-7, 24-34 as currently amended and new claim 35 [Paper No. 26 filed 7/14/2003] are under examination in the instant office action.

Applicants canceled the non-elected claims 2, 3 and 8-23 [Paper No. 26 filed 7/14/2003]. The election was made without traverse [Paper No. 7 filed 1/25/2001]. The non-elected claim 4 was withdrawn from consideration but remains pending. Please, cancel the noted claim to put the application in condition for allowance.

Claim Objections

Claim 6 is objected to because of the following informalities: It appears that there is some typing error. For example: see line 10 of claim 6 wherein there two "and". It is suggested to delete "and" at first occurrence or to make other appropriate correction is required. The appropriate correction is required.

Claim Rejections - 35 USC § 112

Claims 5-7, 24, 28, 29, 33, 34 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 and 6 recite the limitation "improved" solution in correlation with the final volume of the solution for determination of amounts of the solution ingredients (see last lines of these claims). There is insufficient antecedent basis for this limitation in the claims. Claims are drawn to "a solution". Please, amend the claims accordingly to the use of one/same solution by deletion of the phrase "improved", for example. The same rejection is applied to the dependent claims 7, 24, 28, 29, 33, 34 and 35. Please, amend these claims accordingly to claim 5.

Claim 6 is indefinite with regard to the amount of THAM buffer because it recites addition of a particular amount such as 24 "mL" to unidentified volume. Thus, the pH as might have been intended is uncertain.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1 and 33 as amended remain rejected under 35 U.S.C. 103(a) as being unpatentable over Wlakenbach et al. [IDS-12-AO, 1991] taken with Ingemansson *et al.* [IDS-12-AN, 1995], Ingemansson *et al.* [IDS-1, AT-2, 1995], Pinsky *et al.* [IDS-1, AQ-2, 1994] and Naka *et al.* [IDS-1, AT-1, 1995].

Claim 1 is directed to a preservation solution comprising calcium ion, colloidally active substance and nitroglycerin wherein nitroglycerin concentration is 10^{-4} to 10^{-7} M and calcium ion concentration is 0.3-1.5 mM. Claim 33 is further drawn to a method for preserving

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organs or tissues by storing the organs or tissues for 36 hours and more at 0.5-12 C and/or for more than 36 hours at 0.5-12 C in the claimed solution.

The cited references are relied upon as explained in the prior office action and repeated herein in brief.

The cited references by Wlakenbach et al. [IDS-12, AO, 1991], Ingemansson *et al.* [IDS-12, AN, 1995] and Ingemansson *et al.* [IDS-1, AT-2, 1995] clearly teach and/or suggest the preservation solutions comprising combination of calcium ion and colloidosmotically active substance. They also teach methods for preserving organs or tissues by storing the organs or tissues in the preservation solution under conditions as presently claimed. The calcium ion concentration within the presently claimed range 1.5 mM, for example: see the reference by Ingemansson *et al.* [IDS-12-AN, 1995] at table 1.

In particular, the cited reference discloses following. For example: Wlakenbach et al teaches a preservation solution which comprises calcium, about 1-15% of dextran 40, buffer, glucose and ions of potassium, magnesium and sodium. The reference also teaches a method for preserving organs or tissues such as cornea, for example, by storing them in the preservation solution at low temperature including 4 C or between 0.5 and 12 C for a period of time such as about 7 days including time periods such as more than 36 hours and less than 36 hours. The cited references by Ingemansson *et al.* [IDS-12, AN, 1995] and Ingemansson *et al.* [IDS-1, AT-2, 1995] teach the use of various solutions in the methods for preservation of various organs and tissues of animals including tissues with blood vessels, veins, vascular endothelium and/or contractile tissues wherein solutions comprise calcium, colloidosmotically active substance or dextran, glucose, buffer and ions of potassium, magnesium and sodium at various concentrations. The reference by Ingemansson *et al.* [IDS-1, AT-2, 1995] teaches that Perfadex solution comprising colloidosmotically active substance manifests superior effects related to preservation of contractile tissues. The reference by Ingemansson *et al.* [IDS-12, AN, 1995] teaches that

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incorporation of calcium ion into storage or organ-bath solutions resulted in preservation of a contractile capacity of animal tissues for a period of time more than 36 hours and it suggests incorporation of calcium into various preservation solutions including Perfadex, for example (page 1181, col. 1, par. 3).

Thus, the cited references by Wlakenbach et al. [IDS-12, AO, 1991], Ingemansson *et al.* [IDS-12, AN, 1995] and Ingemansson *et al.* [IDS-1, AT-2, 1995] clearly teach and/or suggest the preservation solutions comprising combination of calcium ion and colloidosmotically active substance. But they are lacking teaching drawn to the inclusion of nitroglycerin into solutions and into the solutions for in the methods preservation of animal organs and tissues.

However, the references by Pinsky et al and by Naka et al. clearly teach that incorporation of nitroglycerin into the storage or preservation solutions enhances survival of animal tissue or organ grafts and that nitroglycerin maintains vascular homeostasis in animal organs and tissues stored/preserved in the solutions (see abstracts). The amounts of nitroglycerin are about 0.1 mg/ml as disclosed by Pinsky et al and by Naka et al. The nitroglycerin is added to the calcium ion containing solutions such as Ringer's solution, for example: see references at abstract or at section "Methods"). The references by Pinsky and by Naka are lacking the disclosure about the use of a colloidosmotically active substance in the calcium-containing preservation solutions. However, the cited above references clearly teach the use of colloidosmotically active substance in the calcium-containing preservation solutions.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to include nitroglycerine into the calcium-containing preservation solution, including the calcium-containing solution with both colloidosmotically active substance and calcium, with a reasonable expectation of success in maximizing and/or optimizing the preservation effects for animal organs and tissue because the prior art teaches that incorporation of nitroglycerin into preservation solution provides for maintenance of vascular

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homeostasis in animal organs and for integrity of animal tissues and because the prior art teaches that incorporation of nitroglycerin into the calcium containing preservation solutions enhances survival of animal tissue or organ grafts and because various calcium-containing compositions including colloidally active substance containing solutions are known the prior art as adequately demonstrated by the cited references. One of skill in the art would have been motivated to combine all three ingredients including calcium ion, colloidally active substance and nitroglycerin in the preservation solution because each ingredient is taught by the prior art to be useful for the same purpose such as animal tissue/organ preservation in order to form a third composition useful for the same purpose such as animal tissue/organ preservation. It is well known that it is prima facie obvious to combine **two or more** ingredients each of which is taught by the prior art to be useful for the same purpose in order to form a third composition which is useful for the same purpose. The idea for combining them flows logically from their having been used individually in the prior art. In re Pinten, 459 F.2d 1053, 173 USPQ 801 (CCPA 1972); In re Susi, 58 CCPA 1074, 1079-80; 440 F.2d 442, 445; 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21; 279 F.2d 274, 276-277; 126 USPQ 186, 188 (1960). Thus, the claimed invention as a whole was clearly prima facie obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented by the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 7/14/2003 [Paper No. 26] have been fully considered but they are not all found persuasive for the reasons below.

The Declaration by the inventor Stig Steen that was filed on 4/20/2000 has been reviewed.

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Applicant argues that there is no suggestion to combine the teaching of the cited references. However the references are in the same field of endeavor and seek to solve the same problems as the instant application and claims, and one of skill in the art is free to select the components available in the prior art. In re Winslow, 151 USPQ 48 (CCPA, 1966).

Applicant asserts (response page 8) that the cited prior references and the references by Pinsky and Naka, in particular, fail to teach the use of nitroglycerin in a solution that also contains calcium ions. This is incorrect because the reference by Pinsky and Naka teach incorporation of nitroglycerin into the calcium-containing solution such as, for example: the Ringer' solution that is known to contain about 1 mM of calcium (see US 6,150,409 at col. 7, line 30). Thus, the applicant's argument concerning the lack of teaching in the cited references about incorporation of nitroglycerin into the calcium-containing solutions is incorrect.

Applicant argument regarding the synergistic effect of combining calcium and nitroglycerin in the preservation solution as set forth in the present application and as demonstrated on Figure 1 has been fully considered. However, this argument is not convincing since the value of the combination "Perfadex plus calcium" and the value of the combination "Perfadex plus calcium plus nitroglycerin" fall within the standard deviation bar. The evidence relied upon should establish "...the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." Ex parte Gelles, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter.)

Further, the evidence necessary to overcome a *prima facie* case of obviousness must not only be clear and convincing, but must also be commensurate in scope with the claimed subject matter. The amounts of calcium and nitroglycerin used in the experiment of the Fig. 1 do not delineate clearly the amounts of calcium and nitroglycerin required to obtain the touted synergistic result. Thus, the applicant's showing and arguments do not commensurate in scope with the claimed subject matter. The allegation that limited data is sufficient to establish the

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existence of synergism from other such ingredients is without merit. It is well recognized that synergism is a highly unpredictable result that is very dependent on the ingredients used and the amounts of each. Thus any combination for which synergism is not clearly established would be properly rejected because non-obviousness would not have been established.

Claims 1 and 33 are not allowed.

Claims 5-7, 24-32, 34 and 35 are free from prior art and might be allowable upon resolution of the issues related to the claim objection and rejection under 112-2.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (703) 308-9351. The examiner can normally be reached on Monday to Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vera Afremova

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October 31, 2003

VERA AFREMOVA

PATENT EXAMINER

